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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,180	12/12/2003	Larry Norton	052849.0003	2583

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EXAMINER	
OLSON, ERIC	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 04/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/735,180	NORTON, LARRY	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-39* is/are rejected.

7)☐ Claim(s) *39* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 December 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03/15/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

This application claims benefit of provisional application 60/432840 filed December 12, 2002. Claims 1-39 are pending in this application and examined on the merits herein.

Drawings

The drawings are objected to because the symbols for Doxorubicin and Paclitaxel are indistinguishable in black-and white. The drawing appears to be a black-and-white copy of a color drawing. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required

corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

Claim 39 is objected to because of the following informalities: The claim is not a complete sentence. In particular, it begins with the phrase, In a method for providing chemotherapeutic treatment." It is suggested that the word "in" be deleted from the beginning of the claim. Appropriate correction is required.

Claim Rejections – 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38 and 39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of providing chemotherapeutic treatment for breast cancer involving the specific sequential combination of drugs mentioned in the specification, does not reasonably provide enablement for a method of providing chemotherapeutic treatment for any type of cancer using any chemotherapeutic agent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:
(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The claimed invention is a method for cancer chemotherapy which is an improvement over existing chemotherapeutic methods. The claimed invention is alleged to be an improvement over the prior art in two ways. The first improvement is the administration of the chemotherapeutic agents in a sequential dose-dense protocol, as opposed to a simultaneous combination protocol. The second alleged improvement is the administration of a specific optimized regimen of dose, frequency, and duration of treatment which is claimed to produce improved results.

The state of the prior art: The skilled artisan would view cancer as a group of maladies not treatable with one medicament or therapeutic regimen. No single chemotherapeutic drug is useful for the treatment of every case of cancer. Indeed, some types of cancer to not respond well to any known chemotherapeutic drugs. According to the Merck Manual of Diagnosis and Therapy (Reference included with PTO-892), Hepatocellular carcinomas and renal cell carcinomas are not generally improved by chemotherapy. Acute lymphoblastic leukemia, on the other hand,

responds well to a number of drugs, including vincristine, anthracyclines, and aspariginases, while acute mylogenous leukemia, on the other hand, responds to fewer drugs and is usually treated with cytarabine in combination with daunorubicin or idarubicin. Breast cancer, on the other hand, is best treated with surgery and/or radiation, but the prognosis can be improved by the addition of adjuvant chemotherapy.

Dose-dense chemotherapy is well known in the prior art for the treatment of carcinomas, especially breast cancer. However, it is not widely practiced for the treatment of sarcomas or leukemias.

The relative skill of those in the art: The level of skill in the art is high.

The predictability or unpredictability of the art: As mentioned above, no single treatment is effective for all cancers. Different cancers vary widely in their response to different chemotherapy regimens. According to the Oxford Textbook of Oncology, (Reference cited in PTO-892) "The important criteria for the tumor include its sensitivity to cytostatic drugs, its clinical stage and its mass, the presence of measurable lesions or biochemical markers, and, finally, growth characteristics," as well as, "*In vitro* sensitivity tests have been disappointing. They predict well for resistance but are of little use for sensitivity," (p. 451, right column, second paragraph) and, "For many types of cancer the potential benefit of chemotherapy has not been demonstrated in well-designed clinical trials."

Based on the known teachings of the prior art such as that stated above, one skilled in the art would recognize that it is highly unpredictable in regard to the treatment in the instant case, including treating numerous and various tumors: gynecological

tumors, ovarian carcinomas, testicle tumors, prostate carcinomas, skin cancer, kidney cancer, bladder tumors, esophagus carcinomas, stomach cancer, rectal carcinomas, pancreas carcinomas, thyroid cancer, adrenal tumors, various types of leukemia and lymphomas, Hodgkin's disease, tumor illnesses of the CAN, soft-tissue sarcomas, bone sarcomas, benign and malignant mesotheliomas, especially intestine cancer, liver cancer, breast cancer, bronchial and lung carcinomas, melanomas, acute and chronic leukemias and benign papillomatosis tumors, by performing the necessary experimentation to develop an optimized dose-dense protocol for treating said cancers.

Note that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Additionally, the claims are interpreted to apply to new drugs for which comprehensive pharmacological data, such as optimal dosages and effectiveness against specific cancers, is not yet available.

The Breadth of the claims: Instant claims 38-39 include methods for treatment or any cancer with any chemotherapeutic agent useful for the treatment of said cancer. The only limits are that the therapy must be administered in a dose-dense protocol and that it must be more effective than treatment in a non-dose-dense protocol.

The amount of direction or guidance presented: While the specification and included references give a detailed description, both theoretical and practical, of dose-dense therapy of breast cancer, they fail to give any guidance to one skilled in the art wishing to practice the invention for other sorts of cancers, such as melanomas or

leukemias. In particular, applicant's disclosure does not address whether the effectiveness of dose-dense chemotherapy against resistant tumors could be expected to extend to classes of tumors, such as hepatomas and melanomas, which are not normally responsive to chemotherapy.

The presence or absence of working examples: All of the working examples concern a single intergroup trial studying the effectiveness of sequential dose-dense chemotherapy involving doxorubicin, paclitaxel, and cyclophosphamide for the treatment of breast cancer. No working examples were given for the treatment of other cancers using other drugs.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable art such as chemotherapy. See MPEP 2164.

The quantity of experimentation necessary: In order to use the disclosed information to practice the claimed invention for a wide range of cancers using a wide range of drugs, a skilled practitioner of the art would develop a specific therapeutic regimen involving a specific combination of drugs for each chemotherapy-responsive cancer. This would involve a process of optimizing and testing various regimens *in vivo* for each type of cancer being treated. This process would involve unpredictable experimentation which would constitute an undue experimental burden on the practitioner.

Genetech, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent

protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, especially the unpredictability of the art and the breadth of the claims, Applicants fail to provide information sufficient to practice the claimed invention for the treatment of all types of cancer.

Claim Rejections – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 9, 19, 23-26, 32, and 38-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Hudis et. al. (Reference included with PTO-1449, marked as reference "A" by examiner).

Hudis et. al. describes a course of sequential dose-dense chemotherapy using the same three drugs specified by the claimed invention. In particular, p. 20, Fig. 1 illustrates the course of treatment used, which consisted of three doses of doxorubicin, separated by 21 weeks (14 days) each, three doses of paclitaxel, a taxane, separated by 2 weeks each, and three doses of cyclophosphamide separated by 2 weeks each. The same course of treatment is described on p. 19 left column, under the heading *Treatment Plan*. This course of treatment uses a sequence of drugs identical to that

described in instant claim 1, with an interval between treatments identical to that described in claims 2 and 25, and a number of cycles identical to that described in claims 3, 9, and 26.

Furthermore, the same paragraph mentioned above (p. 18, left column, *Treatment Plan.*) also discloses that, "All nine cycles of chemotherapy were supported by granulocyte colony stimulating factor, 5 μg/kg subcutaneously, administered on days 3 through 10." This step of administering granulocyte colony stimulating factor between chemotherapy steps anticipated the administration of granulocyte colony stimulating factor according to instant claims 23-24.

Thus the aforementioned claims are anticipated by Hudis et. al.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4-8, 10-18, 20-22, 27-31, and 33-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hudis et. al. (Reference included with PTO-1449, marked as reference "A" by examiner), in view of Henderson et al. (reference included with PTO-892).

Hudis et. al. describes a course of sequential dose-dense chemotherapy using the same three drugs specified by the claimed invention. In particular, p. 20, Fig. 1 illustrates the course of treatment used, which consisted of three doses of Doxorubicin, separated by 21 weeks (14 days) each, three doses of Paclitaxel separated by 2 weeks each, and three doses of cyclophosphamide separated by 2 weeks each. The same course of treatment is described on p. 19 left column, under the heading *Treatment Plan*. Furthermore, the same paragraph mentioned above (p. 18, left column, *Treatment Plan.*) also discloses that, "All nine cycles of chemotherapy were supported by granulocyte colony stimulating factor, 5 μg/kg subcutaneously, administered on days 3 through 10." Hudis et al. does not teach the specific doses of 60, 175, and 600 mg/m^2 for doxorubicin, paclitaxel, and cyclophosphamide mentioned in the aforementioned claims, nor does Hudis et. al. teach the administration of said chemotherapy agents in four cycles.

Henderson et al. describes a study (CALGB 9344) comparing several chemotherapy regimens involving Doxorubicin, Paclitaxel, and Cyclophosphamide. These drugs were administered in amounts of 60, 75, and 600 mg/m^2 in four cycles each. Furthermore, the study concluded that escalation of the dose of doxorubicin produced no additional benefit.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teaching of Hudis et. al. by reducing the dosage of the drugs used and increasing the number of cycles in each treatment.

One of ordinary skill in the art would have been motivated to do so in order to avoid administering an excess of these toxic drugs by reducing the dose and to ensure complete eradication of cancer cells by adding a fourth cycle to each treatment.

One of ordinary skill in the art would have reasonably expected success because the reduced doses and increased number of cycles were already known to be effective for the treatment of breast cancer, and because the treatment regimen of the instant invention differs only slightly from that of Hudis et al. Furthermore, determination of exact treatment regimens, including exact dosage and duration of treatment, is within the ordinary skill in the practice of medicine.

Therefore the invention taken as a whole is *prima facie* obvious.

Summary

No claims are allowed in this invention

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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